Table of Evidence Supporting Enablement

U.S. Patent Application Number 09/392,862

Data Source	Delivery Method	Delivery Vehicle	Fragment[1]	Model System	Result
Declaration of Dr. Gruenert (Item 6, p. 3-4)	In Vivo (nasal administration)	Lipofect-amine	786 bp containing wild type exon 10 of mCFTR	Animal model of cystic fibrosis: ΔF508	Successful in vivo gene therapy: functional correction of ion transport to normal ranges in immune competent mice
Prokopishyn et al., manuscript, "Targeted Genome Editing . . .", Exhibit A of 9/26/03	Ex Vivo (human umbilical cord blood stem/progenitor cells engrafted into mice)	Micro-injection	559 bp containing exons 1&2 of β^S-globin gene	Sickle cell anemia: wild type β^A-globin replaced w/ β^S-globin mutation	Successful replacement and engraftment of corrected stem cells into immune deficient mice; replacement at both alleles; sufficient levels of gene conversion to support therapeutic benefit
Goncz et al. manuscript, "Modification of Genomic . . .", Exhibit B of 9/26/03	In Vitro	Micro-injection	559 bp containing exons 1&2 of β^S-globin mutation	Sickle cell anemia: wild type β^A-globin replaced w/ β^S-globin mutation	Successful & stable in vitro replacement of genomic DNA and successful mRNA expression
Goncz et al. 2001, *Gene Therapy* 8:961-965, Exhibit C of 12/3/01	In Vivo (into lungs via intratracheal administration)	1. AVE 2. Lipofect-amine 3. DDAB	783 bp containing exon 10 of mCFTR w/ ΔF508	Animal model of cystic fibrosis: ΔF508	Successful in vivo fragment replacement and stable expression of altered DNA & mRNA
Kunzelmann et al. 1996, *Gene Therapy* 3:859-867, Exhibit D of 12/3/01	In Vitro (into cystic fibrosis epithelial cells)	1. Lipo-somes 2. Poly-amido-amine dendrimers	491 bp containing wild type exon 10 of CFTR	Cystic fibrosis: ΔF508	Successful replacement & correction of defect confirmed in genomic DNA and in mRNA; functional correction of ion transport confirmed by patch clamp
Goncz et al. 1998, *Human Molecular Genetics* 7:1913-1919, Exhibit E of 12/3/01	In Vitro (into primary human airway epithelial cells)	1. Lipo-somes 2. Poly-amido-amine dendrimers	488 nt containing exon 10 of CFTR w/ ΔF508	Cystic fibrosis: ΔF508	Successful fragment replacement & correction of defect confirmed in genomic DNA and in mRNA
Kapsa et al. 2001, *Human Gene Therapy* 12:629-642, Exhibit F of 12/3/01	In Vivo (intramuscular injection) and In Vitro (applied to cultured cells)	1. Lipofect-amine 2. Lipo-fectin	603 bp containing exon 23 of dys gene	Animal model of Duchenne muscular dystrophy: *mdx*	Successful in vivo and in vitro replacement and correction of *mdx* dystrophin mutation in immune competent mice; shown to last up to 28 d in culture and at least 3 wks in vivo.
Goncz et al. 2001, abstract, Technologies for *in situ* Repair . . ., Exhibit G of 12/3/01	In Vitro	Lipid-DNA complexes Micro-injection	Fragments containing β^S-globin mutation	Sickle cell anemia: wild type β^A-globin replaced w/ β^S-globin mutation	Successful in vitro replacement at β-globin locus in hematopoietic cells; Replacement does not require transcription; Stable replacement lasts at least 5 wks

[1] Each fragment includes intronic sequence flanking the indicated exon(s).